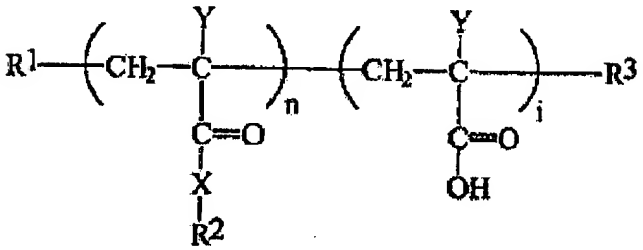
Appln No.: 09/674,191
Amendment Dated: March 12, 2005
Reply to Office Action of December 16, 2004

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A compound of the formula



wherein:
R^1 is a member selected from the group consisting of hydrogen, hydroxyl, amino, optionally-substituted alkyl and a ligand;
Y is a member selected from the group consisting of hydrogen, optionallysubstituted alkyl, optionally-substituted cycloalkyl, optionally-substituted aryl and optionally-substituted heteroaryl;
X is a member selected from the group consisting of optionally-substituted amino, oxygen, sulfur and a carbon single bond;
R_2 is a member selected from the group consisting of ~~hydrogen,~~ C_6 - C_{26} alkyl, C_6 - C_{26} alkenyl, dialkylglycerolyl, dialkenylglycerolyl, diacylglycerolyl, 1,2-diacyl-sn-glycero-3-phosphoethylenyl, 1,2-dialkoxy-3-aminopropanyl and 1,2-diacyloxy-3-aminopropanyl;
R3 is a member selected from the group consisting of hydrogen, hydroxyl, amino, optionally-substituted alkyl and a ligand;
n is greater than 1; and
i is greater than 1.

2. (currently amended) A compound in accordance with claim 1, wherein:
Y is a member selected from the group consisting of hydrogen, optionally-substituted C_1-C_4 alkyl, optionally-substituted C_5-C_6 cycloalkyl and optionally-substituted phenyl;

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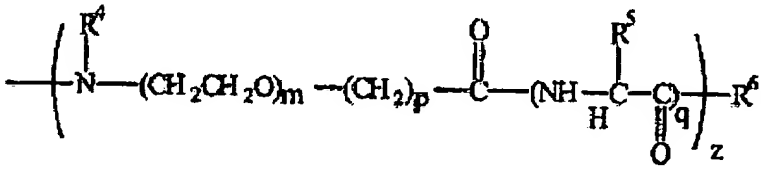
X is a member selected from the group consisting of optionally-substituted amino, oxygen and sulfur;
R^2 is a member selected from the group consisting of ~~hydrogen,~~ C_6-C_{26} alkyl and C_6-C_{26} alkenyl;
n and i, added together, have a sum of ~~about~~ 40 to ~~about~~ 250.

3. (currently amended) A compound in accordance with claim 1, wherein:
Y is a member selected from the group consisting of hydrogen, optionally substituted Cl-C4 alkyl, optionally substituted Cs-C6 cycloalkyl and optionally substituted phenyl;
X is optionally-substituted amino;
R^2 is a member selected from the group consisting of C_6-C_{26} alkyl and C_6 -C_{26} alkenyl;
n and i added together have a sum of ~~about~~ 40 to ~~about~~ 250.

4. (currently amended) A compound in accordance with claim 1, wherein:
Y is a member selected from the group consisting of hydrogen, optionally substituted Cl-C4 alkyl, optionally-substituted C5-C6 cycloalkyl and optionally-substituted phenyl;
X is a carbon single bond;
R^2 is a member selected from the group consisting of dialkylglycerolyl, dialkenylglycerolyl, diacylglycerolyl, 1,2-diacyl-sn-glycero-3-phosphoethylenyl, 1,2dialkoxy-3-aminopropanyl and 1,2-diacyloxy-3-aminopropanyl;
n and i added together have a sum of ~~about~~ 40 to ~~about~~ 250.

5. (currently amended) A compound in accordance with claim 1, wherein:
Y is a member selected from the group consisting of hydrogen, optionally substituted C_1-C_4 alkyl, optionally-substituted C5-C6 cycloalkyl and optionally-substituted phenyl;
X is a carbon single bond;
R^2 is a member selected from the group consisting of dialkylglycerolyl, dialkenylglycerolyl, diacylglycerolyl, 1,2-dialkoxy-3-aminopropanyl and 1,2-diacyloxy3-aminopropanyl; and
n and i, added together, have a sum of ~~about~~ 40 to ~~about~~ 250.

6. (original) A compound in accordance with claim 1, wherein:
R^3 is a ligand, said ligand being a member selected from the group consisting of a lipid, polyethylene glycol and a compound of the formula



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wherein:
R^4 is a member selected from the group consisting of hydrogen and alkyl;
R is a member of the group selected from hydrogen, optionally substituted alkyl, optionally-substituted aryl and a side chain of an amino acid;
R^6 is a member selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, mercapto, hydrazino, amino and NR^7R^8, wherein R^7 and R^8 are independently hydrogen or alkyl;
z is 4 to 80; m is 2 to 6;
p is 1 to 4; and q is 0 or 1.

7. (original) A compound in accordance with claim 1, wherein:
R is a member selected from the group consisting of C_{10}-C_{18} alkyl and C_{10}-C_{18} alkenyl.

8. (original) A compound in accordance with claim 1, wherein:
R^2 is a member selected from the group consisting of dialkylglycerolyl and dialkenylglycerolyl, wherein said dialkyl groups are C_{10}-C_{18} dialkyl and said dialkenyl groups are C_{10}-C_{18} dialkenyl.

9. (original) A compound in accordance with claim 1, wherein:
R^2 is a member selected from the group consisting of diacylglycerolyl and 1,2-diacyl-sn-glycero-3-phosphoethylenyl, wherein said diacyl groups are C_{10}-C_{18} diacyl.

10. (original) A compound in accordance with claim 1, wherein:
R^2 is a member selected from the group consisting of C_{10} alkyl and C_{10} alkenyl.

11. (original) A compound in accordance with claim 1, wherein:
R^2 is a member selected from the group consisting of dialkylglycerolyl and dialkenylglycerolyl, wherein said dialkyl groups are C_{10} dialkyl and said dialkenyl groups are C_{10} dialkenyl.

12. (original) A compound in accordance with claim 1, wherein:
R^2 is a member selected from the group consisting of diacylglycerolyl and 1,2-diacyl-sn-glycero-3-phosphoethylenyl, wherein said diacyl groups are C_{10} acyl.

13. (currently amended) A pH-sensitive liposome, said liposome comprising a lipid and a compound of the formula

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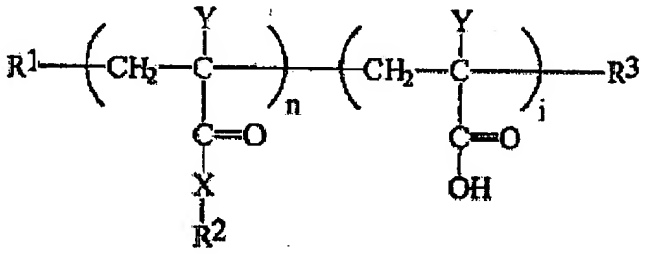

wherein:
R^1 is a member selected from the group consisting of hydrogen, hydroxyl, amino, optionally-substituted alkyl and a ligand;
Y is a member selected from the group consisting of hydrogen, optionallysubstituted alkyl, optionally-substituted cycloalkyl, optionally-substituted aryl and optionally-substituted heteroaryl;
X is a member selected from the group consisting of optionally-substituted amino, oxygen, sulfur a carbon single bond;
R_2 is a member selected from the group consisting of ~~hydrogen;~~ C_6 - C_{26} alkyl, C_6 - C_{26} alkenyl, dialkylglycerolyl, dialkenylglycerolyl, diacylglycerolyl, 1,2-diacyl-sn-glycero-3-phosphoethylenyl, 1,2-dialkoxy-3-aminopropanyl and 1,2-diacyloxy-3-aminopropanyl;
R3 is a member selected from the group consisting of hydrogen, hydroxyl, amino, optionally-substituted alkyl and a ligand;
n is greater than 1; and
i is greater than 1.

14. (original) A pH-sensitive liposome in accordance with claim 13 wherein said liposome is fusogenic.

15. (currently amended) A pH-sensitive liposome in accordance with claim 13 wherein said lipid is a member selected from the group consisting of phosphoglycerides, sphingolipids, phosphatidylcholine, phosphatidylethanolamine, ~~anionic lipids, cationic lipids, noncationic lipids, alternative cationic lipids, neutral lipids,~~ lipolyamines, and cholesterol-based lipids.

16. (original) A pH-sensitive liposome in accordance with claim 15 wherein said lipid is a phosphatidylcholine.

17. (original) A pH-sensitive liposome in accordance with claim 16 wherein said phosphatidylcholine lipid is a member selected from the group consisting of

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distearoylphosphatidylcholine, dipalmitoylphosphatidylcholine, dimyristoylphosphatidylcholine, dilauroylphosphatidylcholine, dioleylphophatidylcholine, hydrogenated egg phosphatidylcholine, soy phosphatidylcholine, hydrogenated soy phosphatidylcholine, and egg phosphatidylcholine.

18. (original) A pH-sensitive liposome in accordance with claim 13 wherein said lipid is a mixture of egg phosphatidylcholine, dimyristoylphosphatidylcholine, dipalmitoylphosphatidylcholine and distearoylphosphotidylcholine.

19. (original) A pH-sensitive liposome in accordance with claim 13 further comprising cholesterol

20. (original) A pH-sensitive liposome in accordance with claim 19 wherein said lipid is egg phosphatidylcholine.

21. (original) A pH-sensitive liposome in accordance with claim 13 further comprising a bilayer stabilizing component.

22. (currently amended) A pH-sensitive liposome in accordance with claim 13 wherein said bilayer stabilizing component is a member selected from the group consisting of lipids, lipid derivatives, detergents, proteins, peptides, polyethylene glycol and N-(.omega.-N'-acetoxy-octa(14'amino-3',6',9',12'-tetraoxatetradecanoyl)) (ATTA). ~~ATTA~~

23. (original) A pH-sensitive liposome in accordance with claim 22 wherein said polyethylene glycol has a molecular weight ranging from about 200 to 10,000.

24. (original) A pH-sensitive liposome in accordance with claim 22 wherein said ATTA has a molecular weight ranging from about 200 to 10,000.

25. (original) A pH-sensitive liposome in accordance with claim 22 wherein said polyethylene glycol has a molecular weight ranging from about 2,000 to 6,000.

26. (original) A pH-sensitive liposome in accordance with claim 22 wherein said ATTA has a molecular weight ranging from about 2,000 to 6,000.

27. (original) A pH-sensitive liposome in accordance with claim 13 wherein said compound is present at a concentration ranging from about 1 weight percent to about 22 weight percent of said lipid

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28. (original) A pH-sensitive liposome in accordance with claim 27 wherein said compound is present at a concentration ranging from about 2 percent to about 20 percent of lipid in a weight to weight ratio.

29. (original) A pH-sensitive liposome in accordance with claim 27 wherein said compound is present at a concentration ranging from about 8 percent to about 10 percent of lipid.

30. (original) A pH-sensitive liposome in accordance with claim 19 wherein said cholesterol is present at a concentration ranging from about 0.02 mole percent to about 50 mole percent.

31. (original) A pH-sensitive liposome in accordance with claim 19 wherein said cholesterol is present at a concentration ranging from about 40 mole percent to about 45 mole percent.

32. (original) A pH-sensitive liposome in accordance with claim 13 wherein said liposome becomes permeable, unstable or fusogenic at a rate which can be controlled by pH
33. A pH-sensitive liposome in accordance with claim 13 wherein said liposome becomes destabilized at a rate which can be controlled by pH.

34. (original) A pH-sensitive liposome in accordance with claim 13 wherein said liposome becomes fusogenic at a rate which can be varied over a pH range of about 3 to about 10.

35. (original) A pH-sensitive liposome in accordance with claim 13 wherein said liposome becomes destabilized at a rate which can be controlled by varying Y

36. (original) A pH-sensitive liposome in accordance with claim 35 wherein Y is different in every other monomer n.

37. (original) A pH-sensitive liposome in accordance with claim 35 wherein Y is different in every other monomer i.

38. (currently amended) A method for delivering a therapeutic compound to a target cell comprising administering to a host containing said target cell a pH-sensitive liposome, said pH-sensitive liposome comprising:
a lipid;
a compound of the formula

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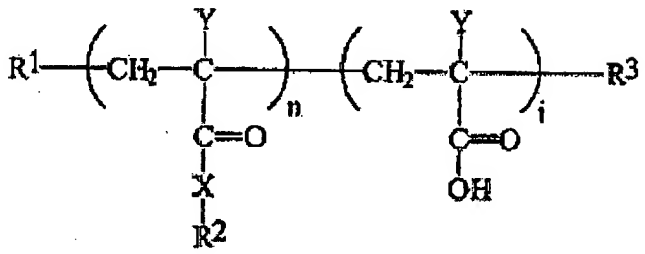

39. (currently amended) A method in accordance with claim 38 further comprising a bilayer stabilizing component, wherein said bilayer stabilizing component is a member selected from the group consisting of lipids, lipid derivatives, detergents, proteins, peptides, polyethylene glycol and ATTA.

40. (original) A method in accordance with claim 38 wherein said liposome further comprises cholesterol.

41. (currently amended) A method in accordance with claim 38 wherein said liposome is fusogenic over a pH range from ~~about~~ 4 to ~~about~~ 7.

42. (original) A method in accordance with claim 38 wherein said liposome is administered intravenously.

43. (original) A method in accordance with claim 38 wherein said liposome is administered parenterally.

44. (original) A method in accordance with claim 38 wherein said liposome administered to said host is unilamellar.

45. (original) A method in accordance with claim 44 wherein said unilamellar liposome has a mean diameter of 0.05 microns to 0.45 microns.

46. (original) A method in accordance with claim 45 wherein said unilamellar liposome has a mean diameter of 0.05 microns to 0.2 microns.

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